Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

08/203,004

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/203,004	02/28/94	BERD	D TJU1156

EXAMINER	
UNGAR, S	

ART UNIT	PAPER NUMBER
1806	22

18M1/1103

PHILIP S. JOHNSON/LORI Y. BEARDELL
WOODCOCK WASHBURN KURTZ
MACKIEWICZ AND NORRIS
ONE LIBERTY PLACE - 46TH FLOOR
PHILADELPHIA PA 19103

1806

DATE MAILED: 11/03/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on Amendment + Declaration filed 8/6/97

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~or thirty days,~~ whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 2, 3, 5-7, 10, 22, 24-28, 34-48 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 2, 3, 5-7, 10, 22, 24-28, 34-48 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☒ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

1. The Amendment and Declaration filed August 6, 1997 (Paper Nos. 20 and 21, respectively) filed in response to the Office Action of February 4, 1997 (Paper No. 18) are acknowledged and have been entered. Previously pending claims 4 and 23 have been cancelled, claims 22, 24 and 36 have been amended and new claims 39-48 have been added. Claims 2, 3, 5-7, 10, 22, 24-28 and 34-48 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

4. Claims 2, 3, 5-7, 10 22, 24-28 and 34-38 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in Paper No. 18, Section 6, pages 2 and 3 and Paper No 7, pages 7 and 8 as they are drawn to "irradiated cells".

Applicant argues that the claims have been amended to recite that tumor cells are "substantially in a no growth phase" to overcome the rejection based on the method and the composition in which the melanoma cells are not "irradiated". The argument has been noted but has not been found persuasive because the specification teaches a melanoma vaccine which consists of irradiated autologous melanoma cells. It would be expected that irradiation would be necessary to prevent the cells from growing following injection and one of skill in the art would not expect that the claimed method would be effective in treating melanoma without using irradiated tumor cells. The specification neither provides guidance for or exemplification of a method of

producing haptenized tumor cells in a "no growth phase" that will maintain this property when injected into a human patient, therefore it could not be predicted from the specification when or whether the haptenized cells would return to a "growth phase" and the method as claimed could result in the wild proliferation of cells that would exacerbate rather than mitigate the tumor and it is not clear whether the method will function as claimed. Therefore, undue experimentation would be required to enable the claims. Applicant's arguments have not been found persuasive and the rejection is maintained.

5. Claims 2, 3, 5-7, 10 22, 24-28 and 34-38 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in Paper No. 18, Section 7, pages 4-5.

Because applicant did not distinctly and specifically point out the supposed errors in the rejection, the rejection is maintained.

6. Claim 25 remains rejected under 35 USC 112, second paragraph for the reasons previously set forth in Paper No. 18, Section 9, pages 7.

Applicant argues that Claim 25 has been amended to refer to "said tumor cell". The argument has been noted but has not been found persuasive because a careful review of Paper No. 20 reveals that, contrary to Applicant's statement, Claim 25 has not been amended in any way. Applicant's arguments have not been found persuasive and the rejection is maintained.

7. All other objections in Paper No. 18 are withdrawn. All other rejections recited in Paper No. 18 are withdrawn due to amendment of the claims to read "syngeneic human tumor cell".

New Grounds of Rejection

Claim Rejections - 35 USC § 112

8. Claims 2, 3, 5-7, 10, 22, 24-28 and 34-48 are rejected under 35 USC 112. first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The new matter referred to is the amendment of the claims 22 and 36 to recite the term "syngeneic" and the addition of claims 39-44, 47 and 48 which also recite the term "syngeneic" . In a telephone interview on October 21, 1997, Lori Beardell pointed to the specification page 4 line 2 as supporting the amendment of the claims to read "syngeneic". The specification discloses that "the potential of lymphocytes elicited by immunization with DNP- or TNP-modified autologous cells to respond to unmodified autologous cells is of considerable interest". A review of Stedman's Medical Dictionary (Williams and Wilkins, Baltimore, 25th Edition, 1990 pages 157 and 1541) reveals that the term "autologous" is defined as "occurring naturally and normally in a certain type of tissue or in a specific structure of the body, sometimes used to denote a neoplasm derived from cells that occur normally at that site" (page 157), while "syngeneic" is defined as "relating to genetically identical individuals" (page 1541). Applicant confirms this definition of "syngeneic" on page 13 of Paper No. 20. It is clear that a pharmaceutical composition comprising haptenized genetically identical human tumor cells is not taught in the specification and therefore it is clear that the subject matter was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

9. The specification is further objected to under 35 USC 112, first paragraph, and Claims 2, 3, 5-7, 10, 22, 24-28 and 34-48 stand rejected under 35 USC 112 first paragraph as failing to provide sufficient guidance to enable one skilled in the art to a make/use a method of treating a malignant tumor in a human patient comprising administering a composition comprising haptenized syngeneic human tumor cells substantially in a no growth phase or a composition comprising a haptenized syngeneic human tumor cell substantially in a no growth phase.

(a) The claims as presently constituted recite administration of "haptenized syngeneic human tumor" cells. However, the specification provides no guidance on or exemplification of how to make "syngeneic human tumor" cells that could be haptenized for administration as a cancer therapy. Syngeneic cells, that is genetically identical cells, have been produced by genetic manipulation of mouse species to produce in-bred strains with genetically identical cells. An in-depth search of the literature has not revealed either a suggestion of or a demonstration that this type of in-breeding to produce genetically identical cells has been contemplated or achieved with humans. Further, the same in-depth search did not reveal either a suggestion of or a demonstration of syngeneic human tumor cells. In view of the lack of guidance from the specification, the known heterogeneity of human cancer cells, and the lack of information in the literature, the invention appears to be not enabled.

(b) Applicant's arguments drawn to irradiated cells noted in Section 4, above, are relevant to the instant rejection of claims 39-48. Claims 39-48 are rejected for the reasons disclosed in Section 4.

10. The specification is further objected to under 35 USC 112, first paragraph, and Claims 45 and 46 are rejected under 35 USC 112 first paragraph as failing to provide sufficient guidance to enable one skilled in the art to a make/use a method of treating a malignant tumor in a human patient comprising administering a composition comprising haptenized syngeneic disrupted human tumor cells or a composition comprising haptenized syngeneic disrupted human tumor cells.

The claims as broadly written read on extracts of the syngeneic human tumor cells including peptides, chemical or cellular extracts. The claims are rejected for the reasons disclosed in Paper No. 7, pages 4-5 and Paper No. 10, pages 4-5 and 9-10. Further, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims as the specification does not provide guidance on or exemplification of haptenized syngeneic disrupted human tumor cells that effectively function as claimed. The claims as broadly written read on haptenized fragmented cells, regardless of size, of all tumor cells. It is not clear from the specification that all fragments of all tumor cells would contain tumor specific antigens. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure that any tumor cell fragment can be haptenized to produce an immunological response that will be effective in

treating cancer. Therefore, undue experimentation would be required to enable the claims.

11. Claims 2, 3, 5-7, 10, 22, 24-28 and 34-48 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 2, 3, 5-7, 10, 22, 24-28 and 34-48 are indefinite because claims 22, 36, 39-44, 47 and 48 recite the phrase "syngeneic human tumor cell". The claims are confusing because, in light of the support for the language pointed to by Applicant as disclosed above, it is not clear what is meant by the term as the support pointed to reads only on autologous cells and there a no definition of the term "syngeneic" in the specification.

(b) Claims 2, 3, 5-7, 10, 22, 24-28 and 34-48 are indefinite because claims 22, 36, 39-44, 47 and 48 recite the phrase "substantially in a no growth phase". The term "substantially" is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Further, the claim is confusing because it appears that some of the cells are not in a "no growth phase". The term is confusing because it is not clear if some or the predominant concentration of the tumor cells are in a no growth phase.

(c) Claims 2, 3, 5-7, 10, 22, 24-28 and 34-48 are indefinite because claims 22, 36, 39-44, 47 and 48 recite the term "haptenized". The claim is confusing because the term is not defined either by the claim or the specification and it is not clear what metes and bounds of patent protection are being sought.

(d) Claims 22, 24-27, 34-35, 39, 40, 43 and 45 are indefinite because claims 22, 34-35, 39, 40 and 43 recite the phrase "having the property". The claims are indefinite because this phrase indicates that the property of eliciting T lymphocytes that infiltrate the tumor of a human is not required.

(e) Claims 45 and 46 are indefinite in the recitation of the term "plurality". The term"plurality" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(f) Claims 45 and 46 are indefinite in the recitation of the phrase "disrupted tumor cell". The claim is confusing because it is not clear whether tumor fragments, peptides, chemicals or cellular extracts are being claimed. Further, the claim is confusing because it is not clear if some or the predominant concentration of the tumor cells are disrupted.

12. No claims allowed.

13. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE

DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached at (703) 308-2731. The fax phone number for this Art Unit is (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 USC 132 or which otherwise require a signature may be used by the applicant and should be addressed to lila.feisee@uspto.gov.

All internet e-mail communications will be made of record in the application file. **PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of USC 122.** This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Serial Number: 08/203,004

Art Unit: 1806

Susan Ungar

October 22, 1997

Lila Feisee
Supervisory Patent Examiner
Group 1800